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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,069	03/14/2007	**Stephen John Kent**	23558-007US	6553

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EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,069	KENT, STEPHEN JOHN	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-79* is/are pending in the application.

4a) Of the above claim(s) *69-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-68 and 73-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/3/09, 3/26/08, 11/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 4/3/09, is acknowledged.
Claims 53-55, 59, 61, 69, and 71-72 have been amended.
Claims 73-79 have been added.
Claims 53-79 are pending.

2. Applicant's election with traverse of group I, drawn a composition comprising antigen presenting cells, claims 53-68 and 73-79, in the reply filed on 4/3/09, is acknowledged. Applicant has further elected peptides as the species of antigen, and peptides that enhance the production of T-helper lymphocytes as the species of peptide.

Applicant's traversal is on the grounds that the antigen presenting cells of Gabrilovich et al. are activated and have been incubated overnight in culture medium. Thus, Applicant concludes that the present claims do not lack unity of invention, because Gabrilovich et al. do not teach the technical feature of an antigen presenting cell that has not been subjected to activating conditions. The antigen presenting cells of Gabrilovich et al. have not been incubated overnight, as asserted by Applicant. Gabrilovich et al. teach contacting freshly isolated antigen presenting cells with an antigen for 45 minutes (i.e. under non-activating conditions and for a time and under conditions that result in an increase of less than about 50% in cell number, see page 2186 in particular). Thus, Gabrilovich et al. teach a method of making an antigen presenting cell identical to the method of claim 69. Thus, the instant claims lack a special technical feature over the prior art of Gabrilovich et al., and unity of invention is lacking.

The requirement is still deemed proper and is therefore made FINAL.

Claims 69-72 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Upon reconsideration, the species of peptide that enhances the production of cytolytic T lymphocyte respons is rejoined. Applicant indicates that claim 58 does not read on the elected invention. However,

claim 58 is being included in the examination, since a peptide can be considered a "proteinaceious" molecule.

Claims 53-68 and 73-79 read on the elected invention and are being acted upon.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

> The oath or declaration is defective because:
> The specification to which the oath or declaration is directed has not been adequately identified. See MPEP § 602. The declaration indicates that the specification was filed as application 10/560,069 on 12/5/05 , but the specification of the '069 application was actually filed on 12/9/05.

4. Claim 53 is objected to for the following informalities: The claim duplicates the phrase "which have not been subjected to activating conditions" in lines 3-4. Correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 53-68 and 73-79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a composition for modulating an immune response in a subject to a target antigen, said composition comprising antigen-presenting cells, including whole blood, fresh blood, or fractions thereof including peripheral blood mononuclear cells, buffy coat fractions of whole blood, irradiated blood, dendritic cells, monocytes, macrophages, lymphocytes, and neutrophils,

does not reasonably provide enablement for:

a composition for modulating an immune response in a subject to a target antigen, said composition comprising precursors of antigen-presenting cells, or comprising packed red cells, natural killer cells, and natural killer T cells.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The instant claims are drawn to a composition for modulating an immune response in a subject to a target antigen, wherein the composition comprises an antigen presenting cells presenting the antigen. Antigen presenting cells including dendritic cells, monocytes/macrophages, and B cells express MHC class II molecules and are known to process and present antigen to T cells (see Vidard et al., 1992). Said APCs are readily available in the blood. Thus blood populations such as PBMC, whole blood, etc. would comprise significant numbers of APCs and could conceivably be used as a source of APC for inducing an immune response. However, the instant claims

encompass compositions comprising non-conventional antigen presenting cells such as red cells, natural killer cells and natural killer T cells. While it is conventional in the art to use antigen presenting cells to induce an antigen specific immune response, red cells, natural killer cells and natural killer T cells are not known as antigen presenting cells. For example, red cells do not even express MHC molecules, and would be unlikely to function to modulate and in vivo immune response to an antigen. Likewise, NK cells are programmed to kill target cells, including antigen presenting cells (see Yu et al., 2006). Additionally, NK T cells are not known to have antigen presenting capacity, and function similarly to T cells (see Song et al., 2009). Furthermore, the claims encompass compositions for modulating an in vivo antigen specific immune response comprising antigen presenting cell precursors. For example, antigen presenting cells such as B cells, develop from, hematopoietic stem cell precursors through a variety of stages (See Janeway and Travers). However, the use of B cell precursors as antigen presenting cells would be highly unpredictable. In fact, B cell precursors can even be susceptible to apoptosis after antigen encounter (see Janeway and Travers, page 5:4).

Thus, given the unpredictability of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The specification provides examples that antigen pulsed PBMC can be used to modulate and antigen specific immune response in vivo. PBMC comprise many types of antigen presenting cells including dendritic cells, B cells, and macrophages. However, the specification does not provide any evidence that other types of non-conventional APCs such as NK cells, NKT cells, or red cells, or antigen presenting cell precursors can function to modulate an antigen specific immune response in vivo. Thus, given the unpredictability of the art, the breadth of the instant claims, and the lack of guidance provided by the instant specification, it would require undue experimentation to make and use the compositions as claimed.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 53-62, 64-68, and 73-78 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 6,080,399.

The '399 patent teaches a composition for inducing an antigen specific immune response in a subject comprising antigen presenting cells, including PBMC, that have been pulsed with peptides (i.e. proteinaceous molecules, see column 4, 7 and 29, in particular). The '399 patent teaches that the PBMC can be freshly isolated and pulsed with peptide by incubating the PBMC with peptide for 1 hr in PBS (see column 41 in particular). Thus, the peptide pulsed PBMC have not been activated, since they have been incubated in PBS in the absence of cytokines or other activation stimuli. Additionally, the PBMC, after only a 1 hour incubation, would inherently have increased less than about 5% in cell number, since they have been processed under identical conditions to those recited in the instant claims. The '399 patent teaches peptides derived from tumor proteins (i.e. proteins expressed by cancer cells, see column 4-5, in particular). The '399 patent teaches that the APCs can be loaded with more than one peptide fragment of an antigen (i.e. a "set" of peptides, see columns 4-5 in particular). The '399 patent also teaches that the peptides can comprise more than one fragment of more than 1 type of protein antigen (i.e. a least 2 "sets" of peptides derived from a distinct polypeptide or non-overlapping peptides, see column 4-5 in particular). The '399 patent also teaches using peptides that bind to class I MHC or class II MHC molecules (i.e. peptides selected to enhance a cytolytic T lymphocyte or T helper lymphocyte response). The '399 patent also teaches using a plurality of distinct peptides with different amino acid substitutions (i.e. peptides displaying partial sequence identity or overlapping peptides that comprise "different" portions of an amino acid sequence of a single polypeptide, see column 22 in particular). Additionally, the '399 patent teaches that only certain, but not most, amino acids should be substituted (i.e. less than 50%). Thus, the substituted peptides have been "derived from" at least 30% of the starting peptide (i.e. a polypeptide of interest).

Thus, the reference clearly anticipates the invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 53-68 and 73-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,080,399, in view of Jager et al., 2000.

The teachings of the '399 patent are described above.

The '399 patent does not teach peptides of 12 to 20 amino acids or peptides wherein the sequence identity is contained at one or both ends of an individual peptide.

Jager et al. teach that vaccination protocols which include MHC-II binding peptides are advantageous, since said peptides stimulate CD4+ T cells which enhance the overall anti-tumor immune response by various helper functions of the CD4+ T cells (see page 629 in particular). Jager et al. further teach several specific 18mer overlapping tumor peptides (i.e. peptides with sequence identity at one end) derived from a NY-ESO tumor antigen which stimulate CD4+ T cells (see page 627 in particular). Jager et al. also teach that NY-ESO is highly immunogenic and is regarded as a promising target for immunotherapeutic interventions in cancer (see page 628 in particular).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include the NY-ESO peptides taught by Jager et al., as peptide fragments for pulsing the PBMC compositions for inducing an anti-tumor immune response of the '399 patent. The ordinary artisan would have been motivated to do so, since Jager et al. teach that the CD4 inducing peptides are derived from a highly immunogenic and promising tumor antigen, and that the induction of an anti-tumor CD4+ T cell response is advantageous since it provides key helper functions that enhance the overall anti-tumor immune response.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes whose telephone number is 571-272-4471. The examiner can normally be reached on 7am to 3:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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